

REMARKS

By the present amendment, claim 1 has been amended to clarify that the model mouse is a model for human psychiatric disorders with deficient function of PACAP gene.

Claims 1-6 and 14-18 are pending in the present application. The claims are directed to a model mouse for human psychiatric disorders with deficient function of PACAP gene.

In the Office Action of September 8, 2004, claims 1-18 were rejected under 35 U.S.C. 112, first paragraph, as not enabled.

It was alleged in the Office Action (i) that use “for studying the in vivo function of PACAP-dependent signaling in pathological disorders” or use as “a psychiatric model” are not “real world use”, (ii) that the “methods such as random integration or RNAi” are not enabled because disruption of the endogenous PACAP gene is “unpredictable”, (iii) that the unpredictability of the claimed method as applied to heterozygous animals lies in the resulting phenotype rather than in the successful application of the method itself, and (iv) that there is no evidence of a connection between psychiatric disorders and PACAP disruption in humans, only in mice.

Further, in the Advisory Action dated February 28, 2005, it was alleged that “the claimed mouse is not a valid model for any human psychiatric disorder” and that “[i]t is unclear whether human with the same disclosed phenotype is result from the disruption of the PACAP gene.”

Reconsideration and withdrawal of the rejection is respectfully requested. Further to the explanations set forth in the response filed March 8, 2005, Applicants submit that the presently claimed model mouse is useful because it is a valid model of human psychiatric disorders with deficient function of PACAP gene. In other words, the use of the presently claimed model mouse

is not simply to study which phenotype may result from the disruption of the PACAP gene in the model mouse, as alleged in the Advisory Action, but to study human psychiatric disorders that are associated with dysfunction in human PACAP gene, by the use of the model mouse. As a result, the model mouse has a substantial, specific, and credible use that is not simply to further the study of the model mouse itself.

In order to confirm the validity of the model mouse as a model of human psychiatric disorders, the following documents are submitted for consideration:

- Davids et al., Brain Res. Rev. 42, 1-21 (2003)
- Solanto, Bhav. Brain Res. 94, 127-152 (1998)
- Solanto, Neurosci. Biobehav. Rev. 24, 27-30 (2000)
- Gainetdinov et al., Science 283, 297-401 (1999)
- Gainetdinov et al., Mol. Med. Today 6, 43-44 (2000)
- Swerdlow et al., Schizophr. Bull. 24, 285-301 (1998)
- Lipska et al., Neuropsychopharmacology 23, 223-239 (2000)
- Kilts, Biol. Psychiatry 50, 845-855 (2001)

These publications show that mice and humans are well known to react similarly with respect to their psychomotor behavior, and that mice are generally considered as a valid model for psychiatric disorders. Accordingly, it is submitted that a person of the art would immediately recognize that a model mouse that has a PACAP gene deficiency and exhibits altered psychomotor behavior is a valid model for human psychomotor behaviors associated with dysfunction of human PACAP gene. This is a specific and substantial use because the present invention makes it possible to identify for such human pathological disorders, and study and develop treatment. This

use is credible because of the widely recognized use of mice to model human psychomotor behavior, as evidenced by the documents.

In particular, the Lipska article explains that “[a]nimal models are important developments in investigations of the mechanisms underlying a human disease and the design of new treatments” (see Lipska at page 223, left col., first three lines).

Also, the Kilts article provides a review of model animal including gene knockout models. The Kilts article, not only confirms the correlation mouse-humans with respect to behavioral dysfunctions, but also, since the present inventors have established the correlation between the PACAP gene dysfunction and specific behavioral phenotype, the Kilts article confirms the usefulness of a PACAP gene knockout mouse exhibiting behavioral phenotypes as a model for human behavioral phenotype caused by human PACAP gene dysfunction (see in particular Kilts at page 851, left col.).

In this respect, it is submitted that the above publications validate the experimental results established in the present specification regarding the predictability of the claimed method and resulting phenotype, and the connection between psychiatric disorders and PACAP disruption in mice as well as in humans.

By analogy to the examples cited in MPEP 2107.01, the use of the present invention is not to do “[b]asic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved,” because the model mouse is useful, not simply to study the mouse itself, but to study human pathologies. More specifically, the PACAP gene dysfunction in the present model mouse correlates with the onset of psychomotor behaviors identified in the present specification, which is applicable to human psychomotor behavior since

mice are well known models for human psychiatric pathologies.

Thus, the model mouse is useful to identify sources and patterns of human psychiatric pathologies involving PACAP gene deficiencies and to define prevention and treatment measures, much like “[a]n assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition” would also define a ‘real world’ context of use in identifying potential candidates for preventive measures or further monitoring.”

See MPEP 2107.01.

In view of the above, it is submitted that the rejection should be withdrawn.

In conclusion, the invention as presently claimed is patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

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In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 50-2866.

Respectfully submitted,

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